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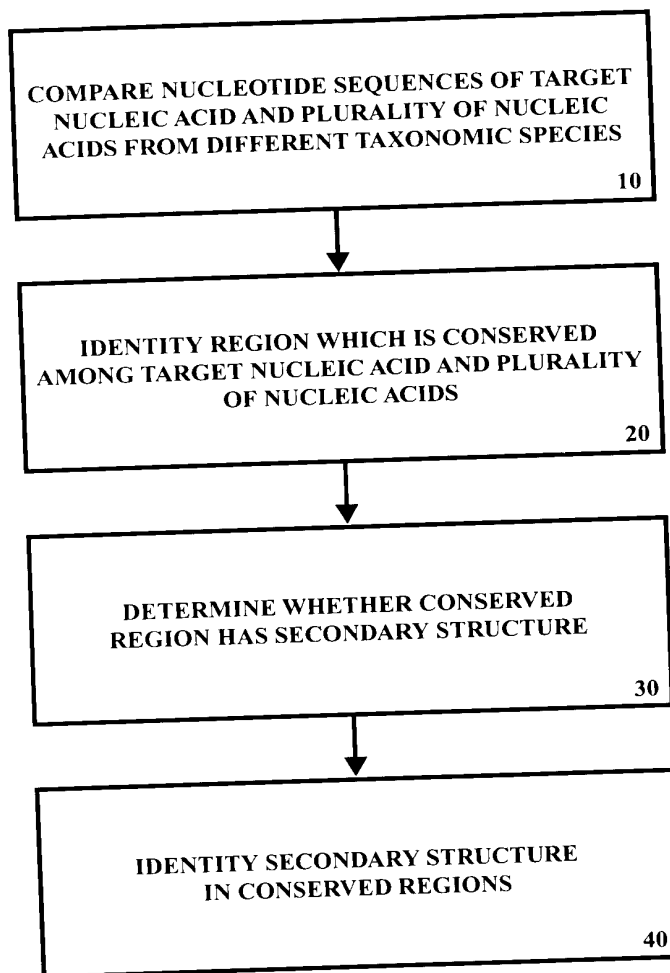


FIGURE 1



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**Find Neighbors
and Assemble
Flow Diagram**

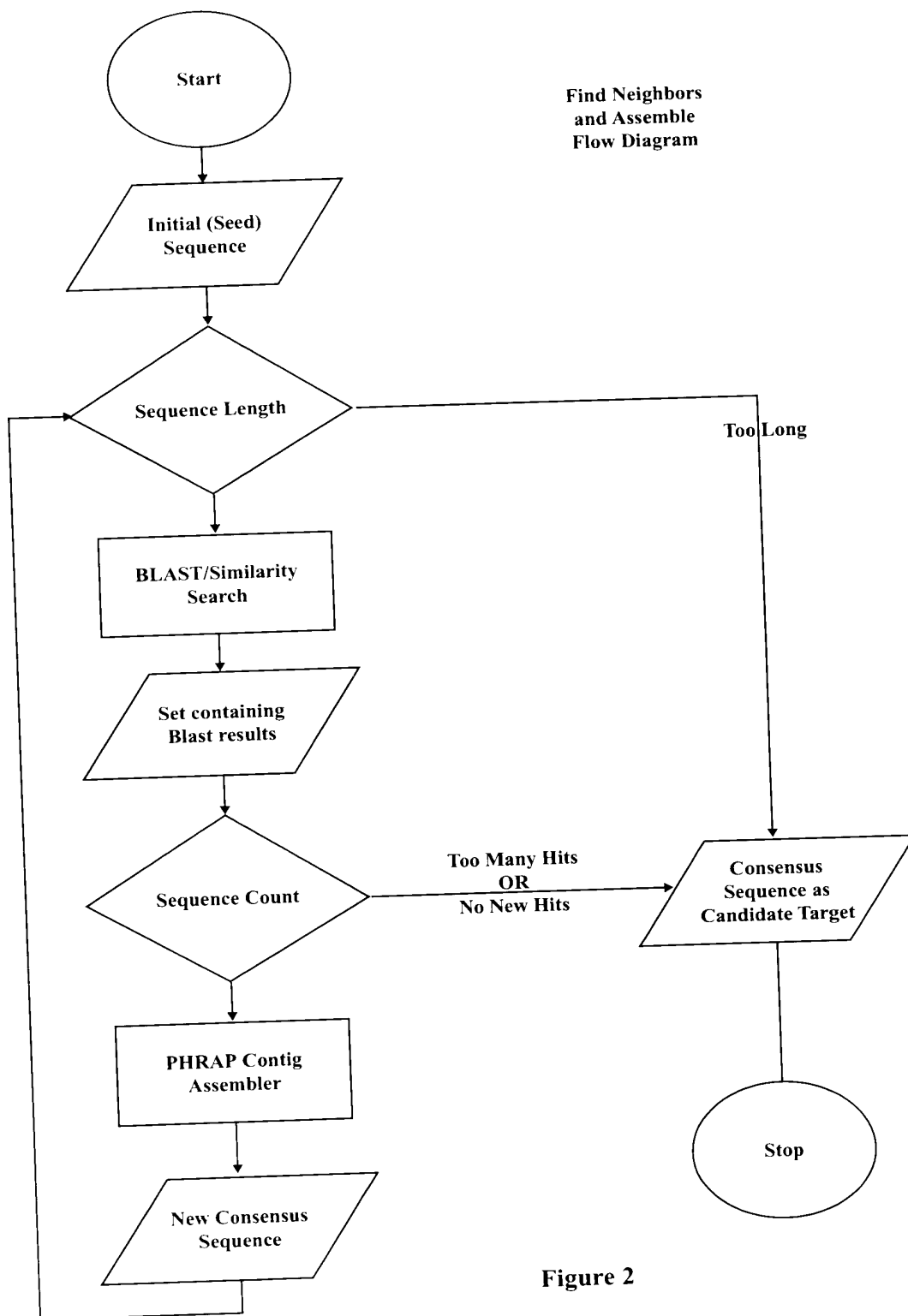
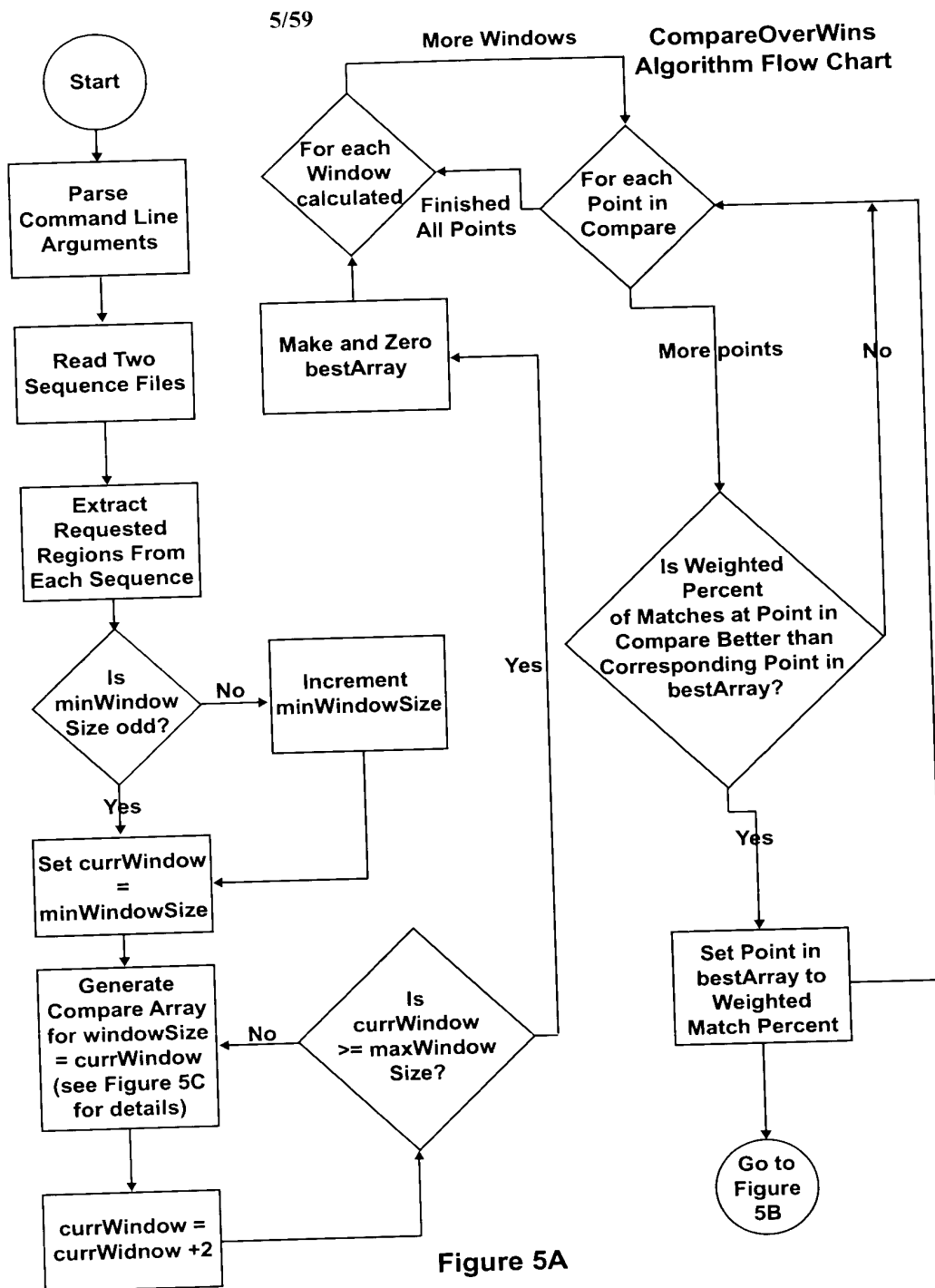


Figure 2





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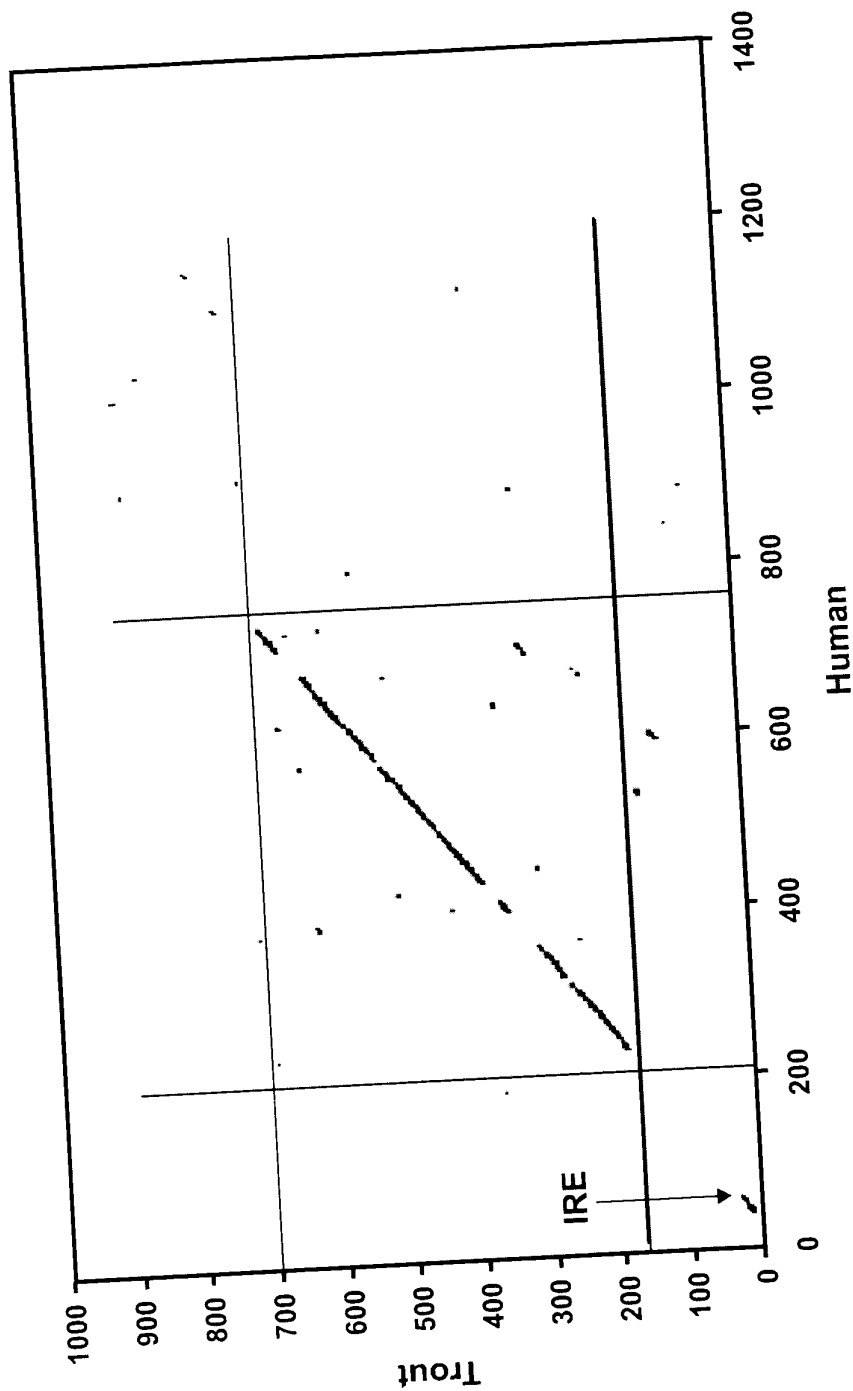


Figure 11



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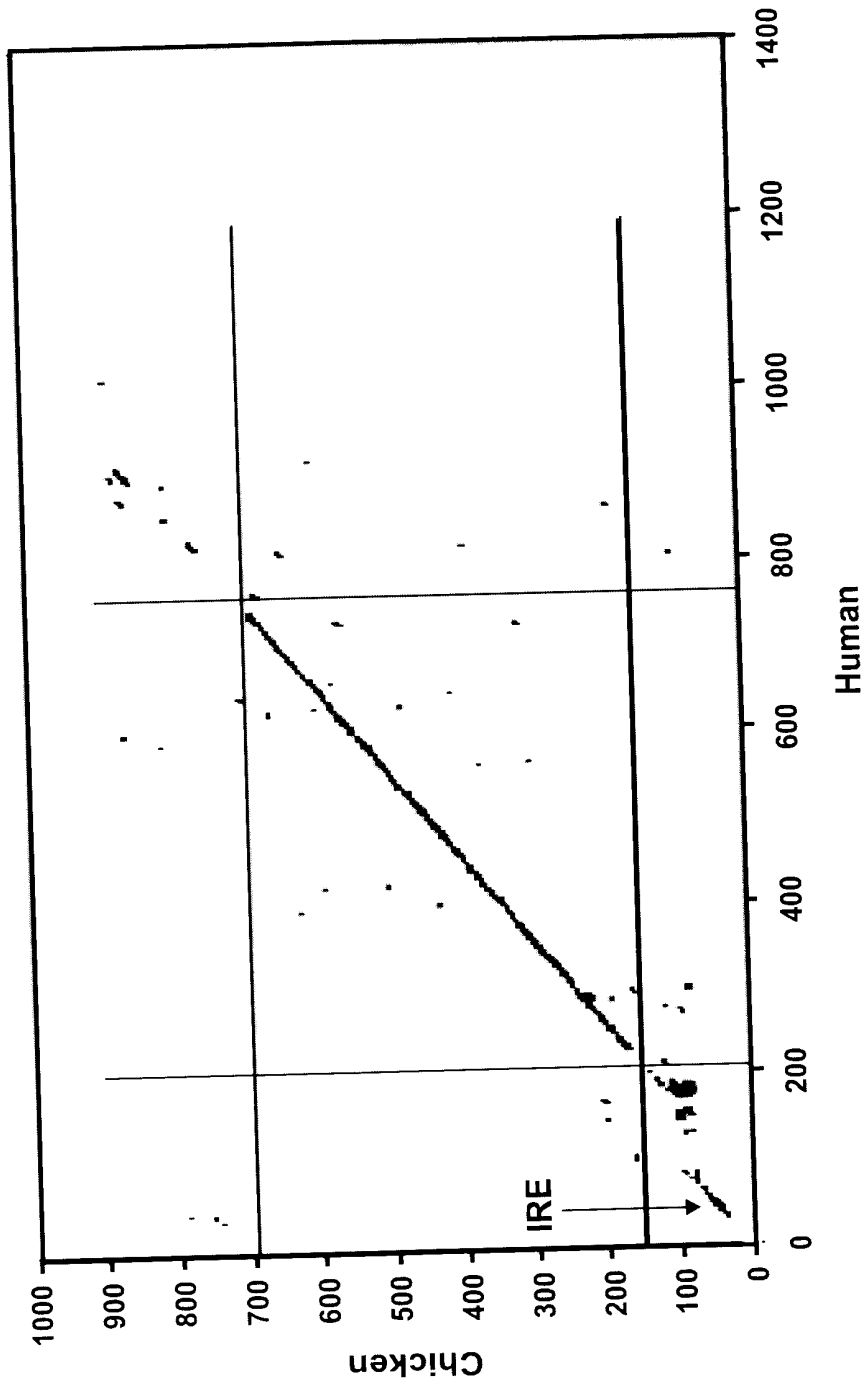


Figure 12



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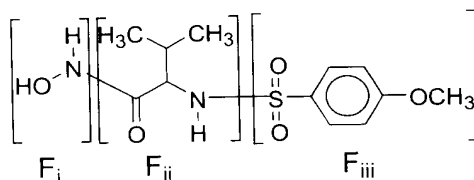
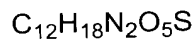
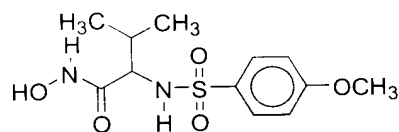
	HUMAN PIG	HAMSTER MOUSE RAT	CHICKEN	TROUT SALMON	XENOPUS FROG	FLY	MOSQUITO
	GU A G C C	GU A G C C	GU A G C C	GU A G C C	GU A G C C	GU A G C C	GU A G C C
	A-U A-U C-G U-G U-A C	A-U A-U C-G U-A U-A C	A-U A-U C-G U-G G-A C	A-U A-U C-G U-A U-A C	A-U A-U C-G U-A U-A C	A-U A-U C-G U-A U-A C	A-U A-U C-G U-A U-A C
	G-C U-G C-G	G-C U-G C-G	G-C U-G C-G	G-C U-G U-G	G-C U-G U-G	G-C U-A U-A C-G	G-C U-A U-A C-G
HUMAN PIG	NO	NO	YES	YES	YES	NO	NO
HAMSTER MOUSE RAT		NO	YES	YES	YES	NO	NO
CHICKEN			NO	YES	YES	NO	NO
TROUT SALMON				NO	YES	YES	YES
XENOPUS FROG					NO	YES	YES
FLY						NO	YES
MOSQUITO							NO

Figure 13



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Compound CI



Molecular Formula

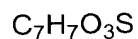
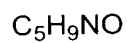


Figure 14

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Addition of fragments to yield compounds

Table

Fragment Identifier	Structure	Name	Molecular formula	Other
F _i		Hydroxylamine	H ₂ NO	...
F _{ii}		Amino acid	C ₅ H ₉ NO	...
F _{iii}		Sulfonyl	C ₇ H ₇ O ₃ S	...

Figure 15



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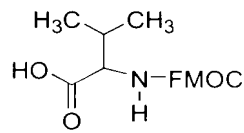
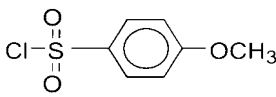
Reagents	Identifier	Name	Properties
$\text{H}-\text{O}-\text{NH}_2$ or $\textcircled{\text{P}}-\text{O}-\text{NH}_2$	R_i	Hydroxylamine	...
	R_{ii}	FMOC blocked amino acid	...
	R_{iii}	Sulfonylchloride	...
$\textcircled{\text{P}}$ = solid support			

Figure 16

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Transformation

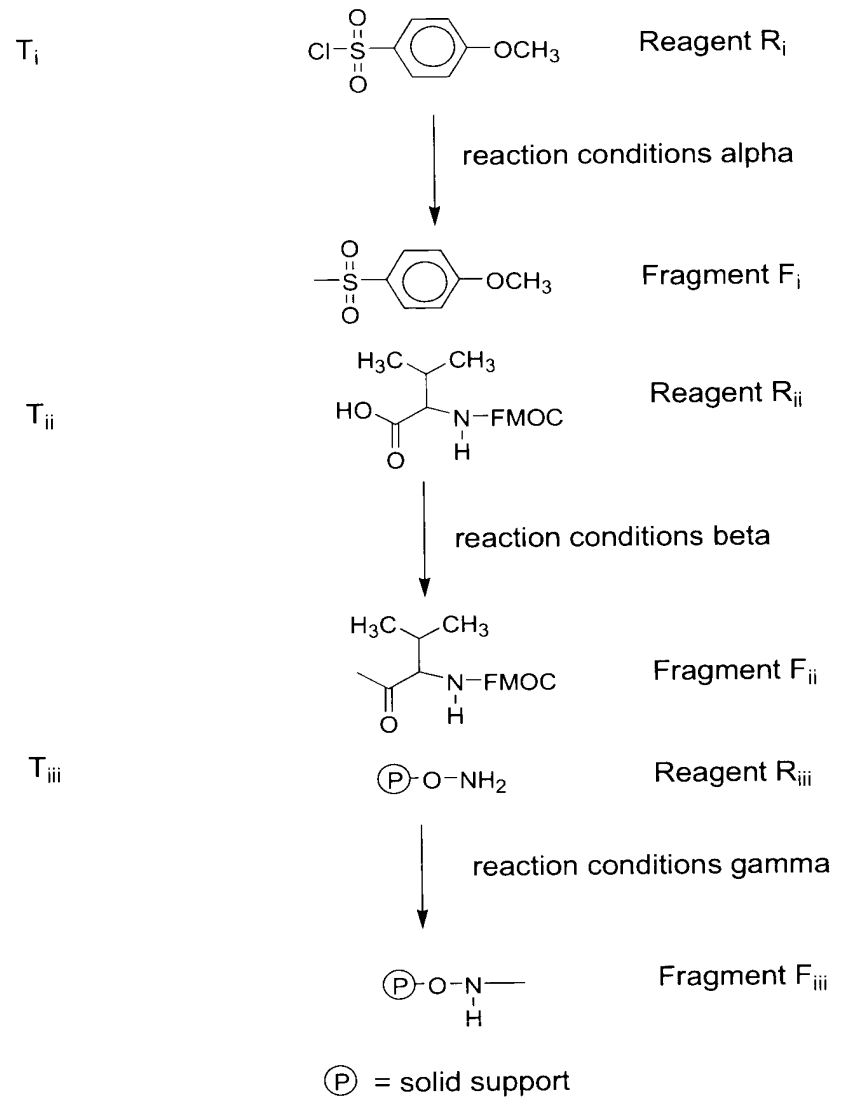


Figure 17



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Common Fragment/Different Reagents and Transformations

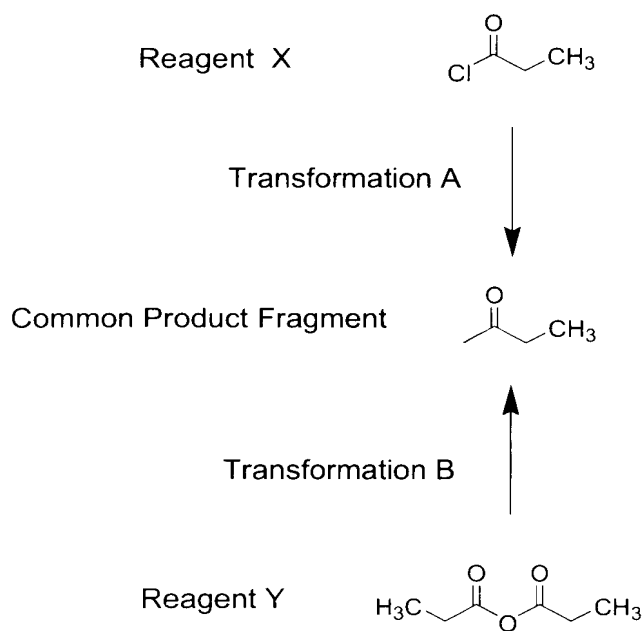
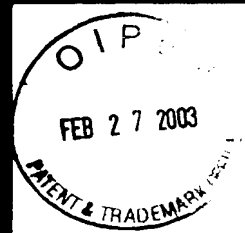


Figure 18



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Common Fragment/Different Reagents and Transformations

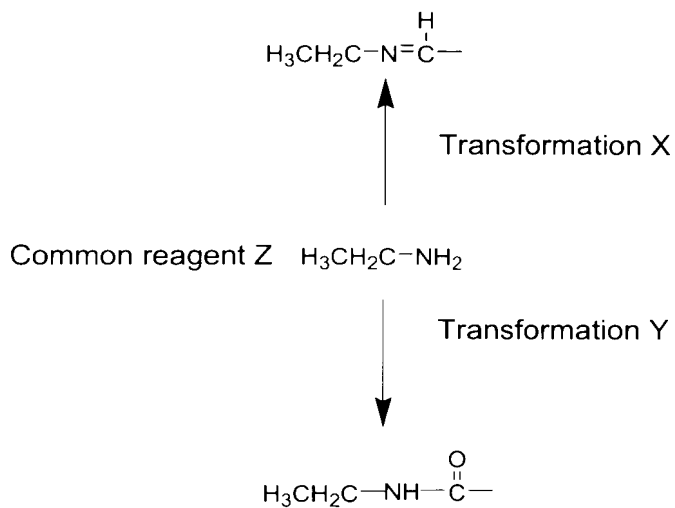
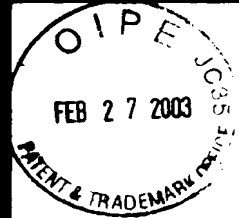


Figure 19A



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Common Reagent

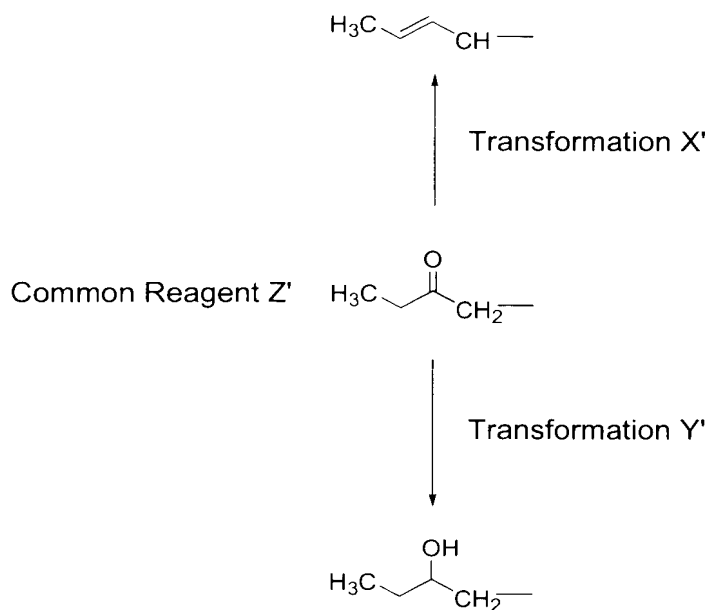


Figure 19B



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Symbolic addition of fragments to yield compound

<u>Symbolic Structure</u>	<u>Symbolic Identifier</u>	<u>Molecular formula</u>
---------------------------	----------------------------	--------------------------

Fragment



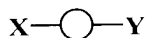
F_i'

C_uH_vN_w ...



F_{ii}'

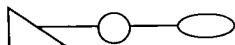
C_uH_vN_w ...



F_{iii}'

C_uH_vN_w ...

Compound



CI'

C_uH_vN_w ...

Molecular formula F_i'

+

Molecular formula F_{ii}'

+

Molecular formula F_{iii}'

= Molecular formula CI'

Figure 20

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Symbolic Reagent Table

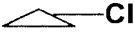
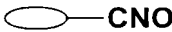


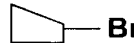
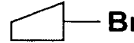
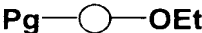
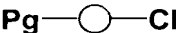
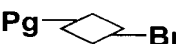
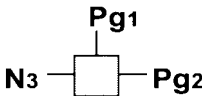
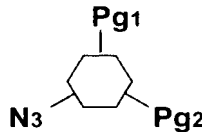
<u>Identifier</u>	<u>Name</u>	<u>Structure</u>	<u>Molecular formula</u>
R1	xxx		xxx
R2	...		...
R3	...		...
R4	...		...
R5	...		...
			
R6	...		...
R7	...		...
R8	...		...
R9	...		...
R10	...		...

Figure 21



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Symbolic Fragment Table



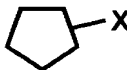
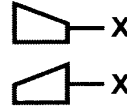


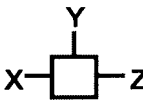
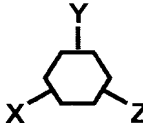
<u>Identifier</u>	<u>Symbolic Sturcture</u>	<u>Molecular Formula</u>	<u>Molecular Weight</u>
F1		XXX	XXX
F2	
F3	
F4	
F5	
F6	
F7	
F8	

Figure 22



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Symbolic Transformation Table



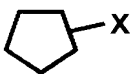
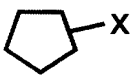







Identifier		Symbolic Reactions		Reagent
T1	F1	 X	← R1	conditions α
T2	F2	 X	← R2	conditions β
T3	F3	 X	← R3	conditions α
T4	F3	 X	← R4	conditions α
T5	F4	 X  X	← R5	conditions α
T6	F5	X-  -Y	← R6	conditions ε
T7	F5	X-  -Y	← R7	conditions α
T8	F6	X-  -Y	← R8	conditions α
T9	F7	X-  -Z	← R9	conditions γ
T10	F8	X-  -Z	← R10	conditions γ

Figure 23



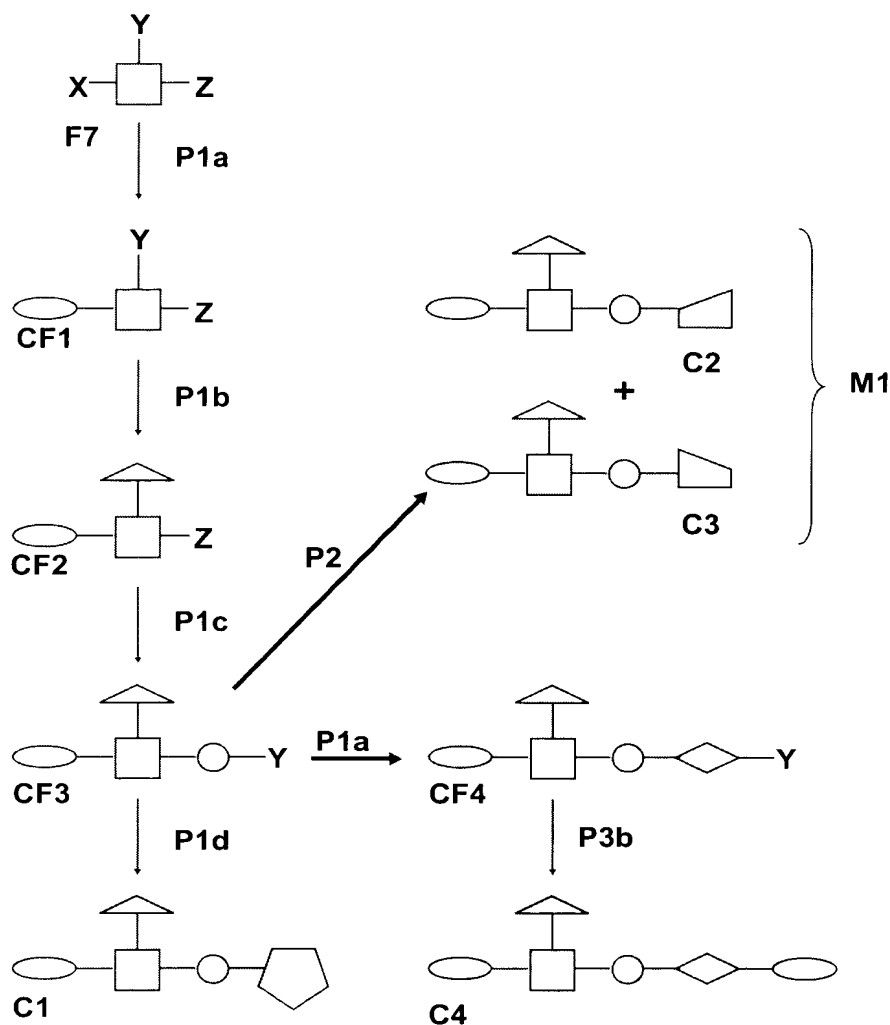
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Single Compounds and Mixtures

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P = synthetic path CF = complex fragment
F = fragment M = mixture
C = compound

Figure 24

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Mixture 2

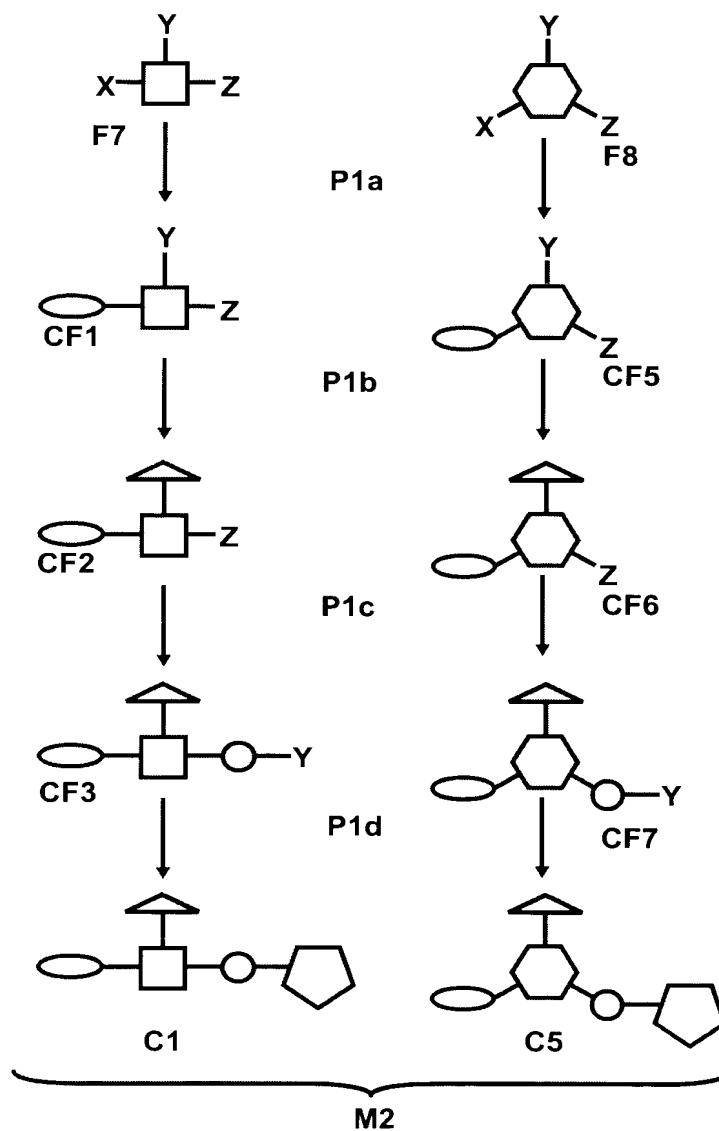


Figure 25



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Mixture 3

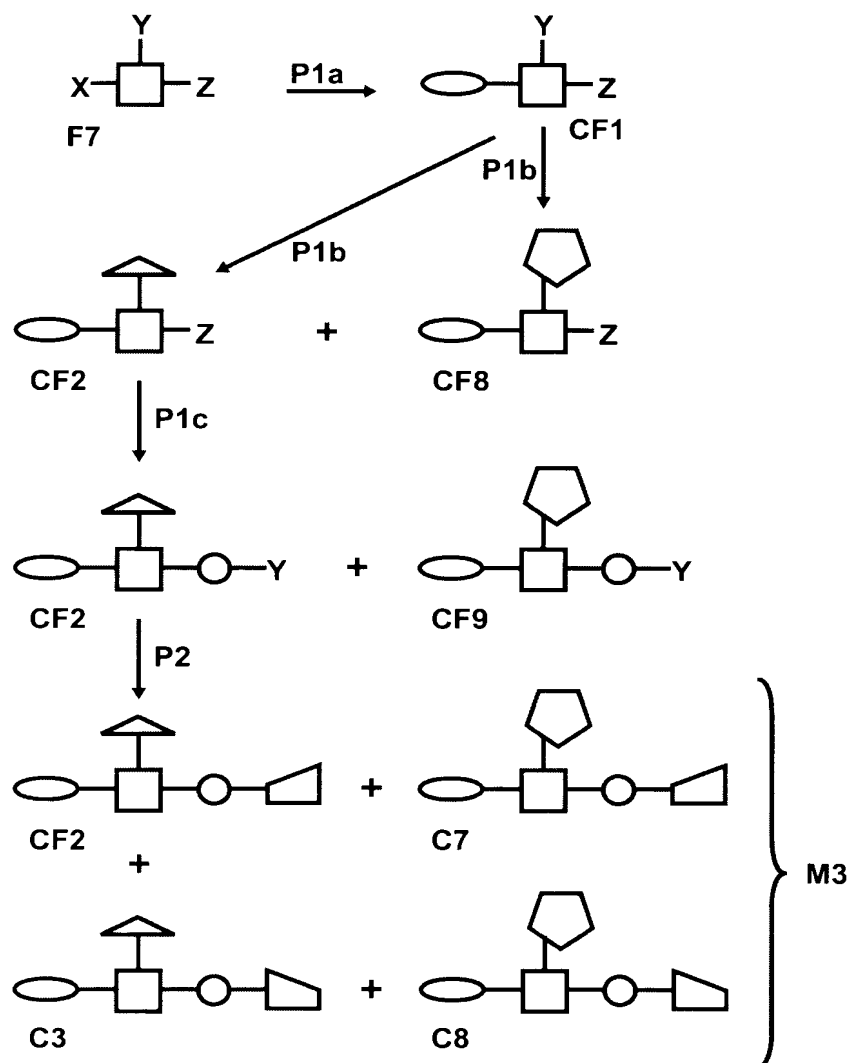


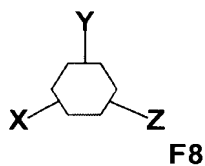
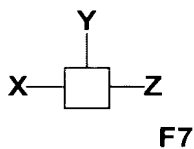
Figure 26



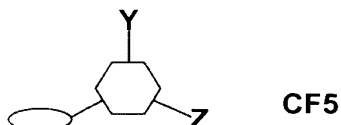
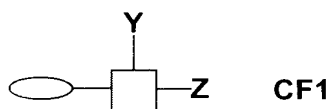
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Mixture 4

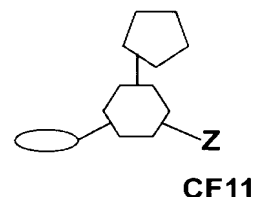
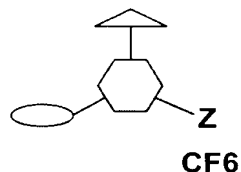
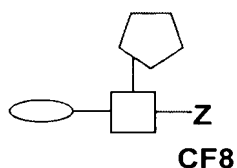
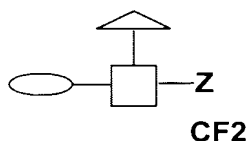
2 Starting Fragments



2 Complex Fragments



4 Complex Fragments



8 Complex Fragments

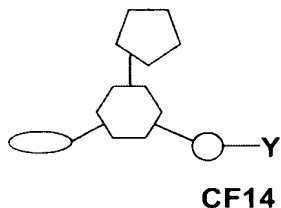
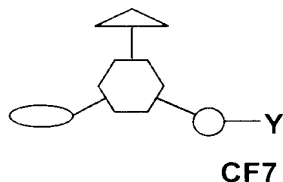
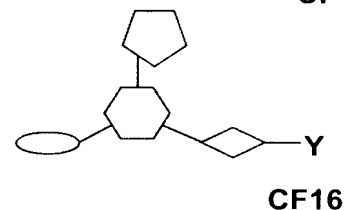
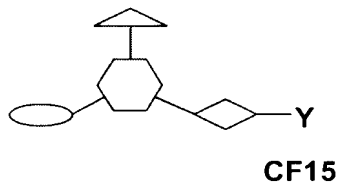
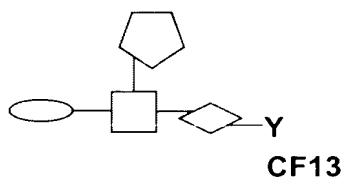
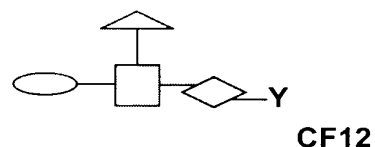
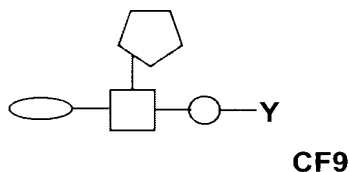
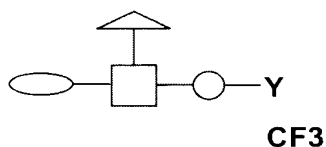


Figure 27A

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Mixture 4 (continued)

16 compounds

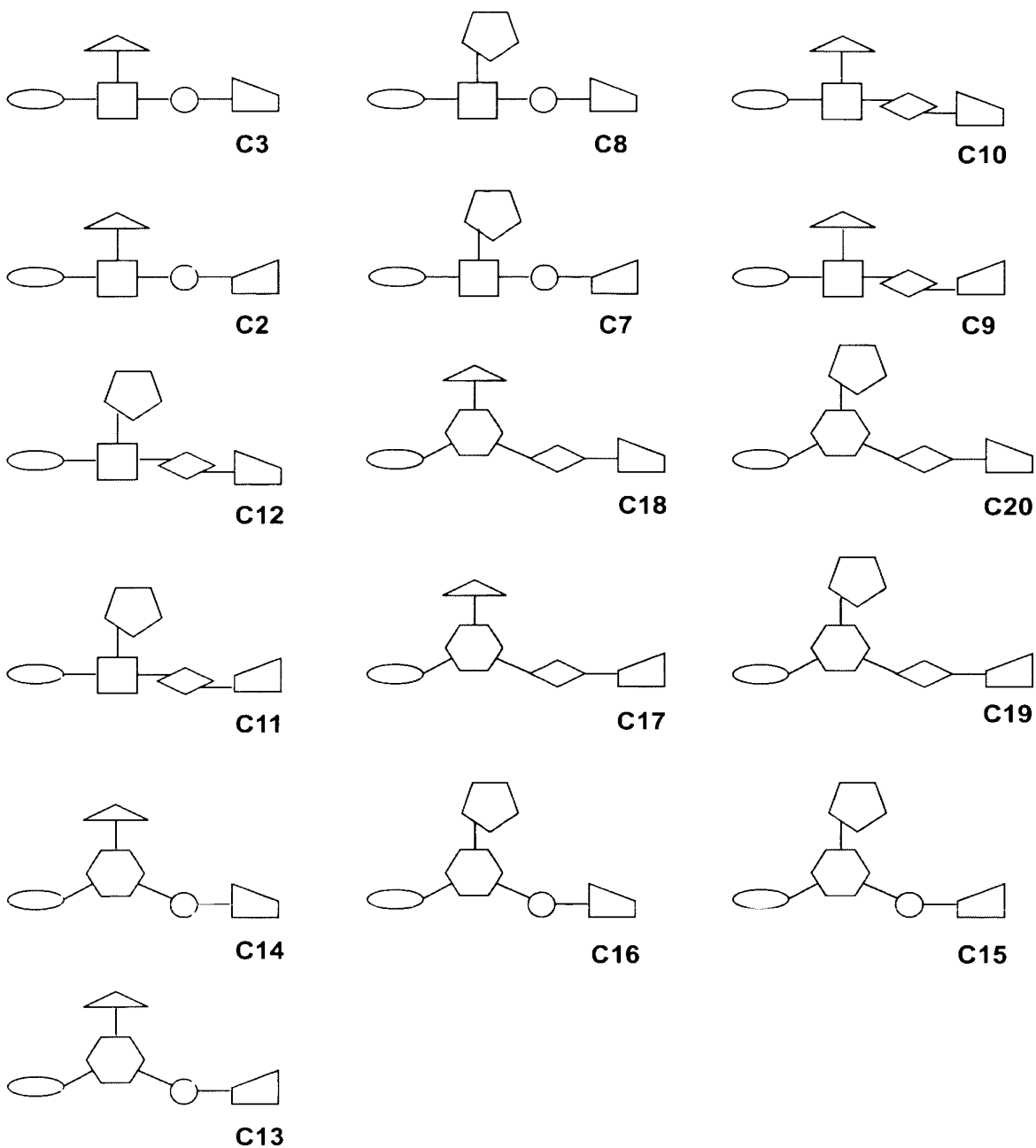


Figure 27B



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Tracking Table for Compound C1

(a) By Fragments:

n	n+1	n+2
F7	F2 F1 F5	F3

(a) By Transformations:

Synthesis Path 1

n	n+1	n+2
T9	T2 T1 T6	T3

Synthesis Path 2

n	n+1	n+2
T9	T2 T1 T7	T3

Synthesis Path 3

n	n+1	n+2
T9	T2 T1 T6	T4

Synthesis Path 4

n	n+1	n+2
T9	T2 T1 T7	T4

Figure 28



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Tracking Table

Tracking M1

Step 1		
T9		
Step 2		
T9	T2	
Step 3		
T9	T2 T1	
Step 4		
T9	T2 T1 T7	
Step 5		
T9	T2 T1 T7	T5 ¹
C2		
Step 5		
T9	T2 T1 T7	T5 ²
C3		

Figure 29



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Tracking Table

Tracking M2

Step 1		
n	n+1	n+2
T9		

Step 2		
n	n+1	n+2
T9	T2	

Step 3		
n	n+1	n+2
T9	T2 T1	

Step 4		
n	n+1	n+2
T9	T2 T1 T7	

Step 5		
n	n+1	n+2
T9	T2 T1 T7	T4

C1

Step 1		
n	n+1	n+2
T10		

Step 2		
n	n+1	n+2
T10	T2	

Step 3		
n	n+1	n+2
T10	T2 T1	

Step 4		
n	n+1	n+2
T10	T2 T1 T7	

Step 5		
n	n+1	n+2
T10	T2 T1 T7	T4

C5

Figure 30

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Tracking Table

Tracking M3

Step 1

T9		
----	--	--

Step 2

T9	T2	
----	----	--

Step 3

T9	T2 T1	
----	----------	--

Step 3

T9	T2 T3	
----	----------	--

Step 4

T9	T2 T1 T7	
----	----------------	--

Step 4

T9	T2 T3 T7	
----	----------------	--

Step 5

T9	T2 T1 T7	T5 ¹
----	----------------	-----------------

C2

Step 5

T9	T2 T1 T7	T5 ²
----	----------------	-----------------

C3

Step 5

T9	T2 T3 T7	T5 ¹
----	----------------	-----------------

C7

Step 5

T9	T2 T3 T7	T5 ²
----	----------------	-----------------

C8

Figure 31

OIP

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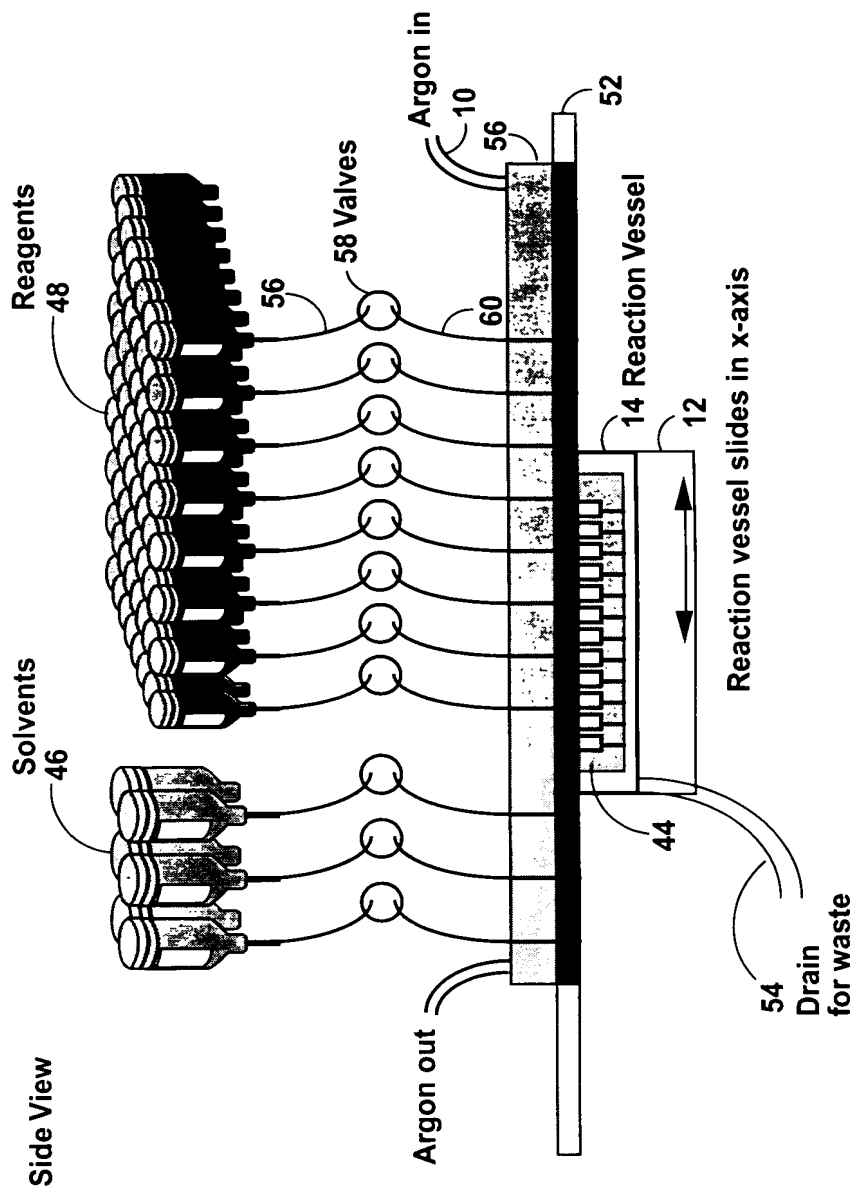


Figure 32

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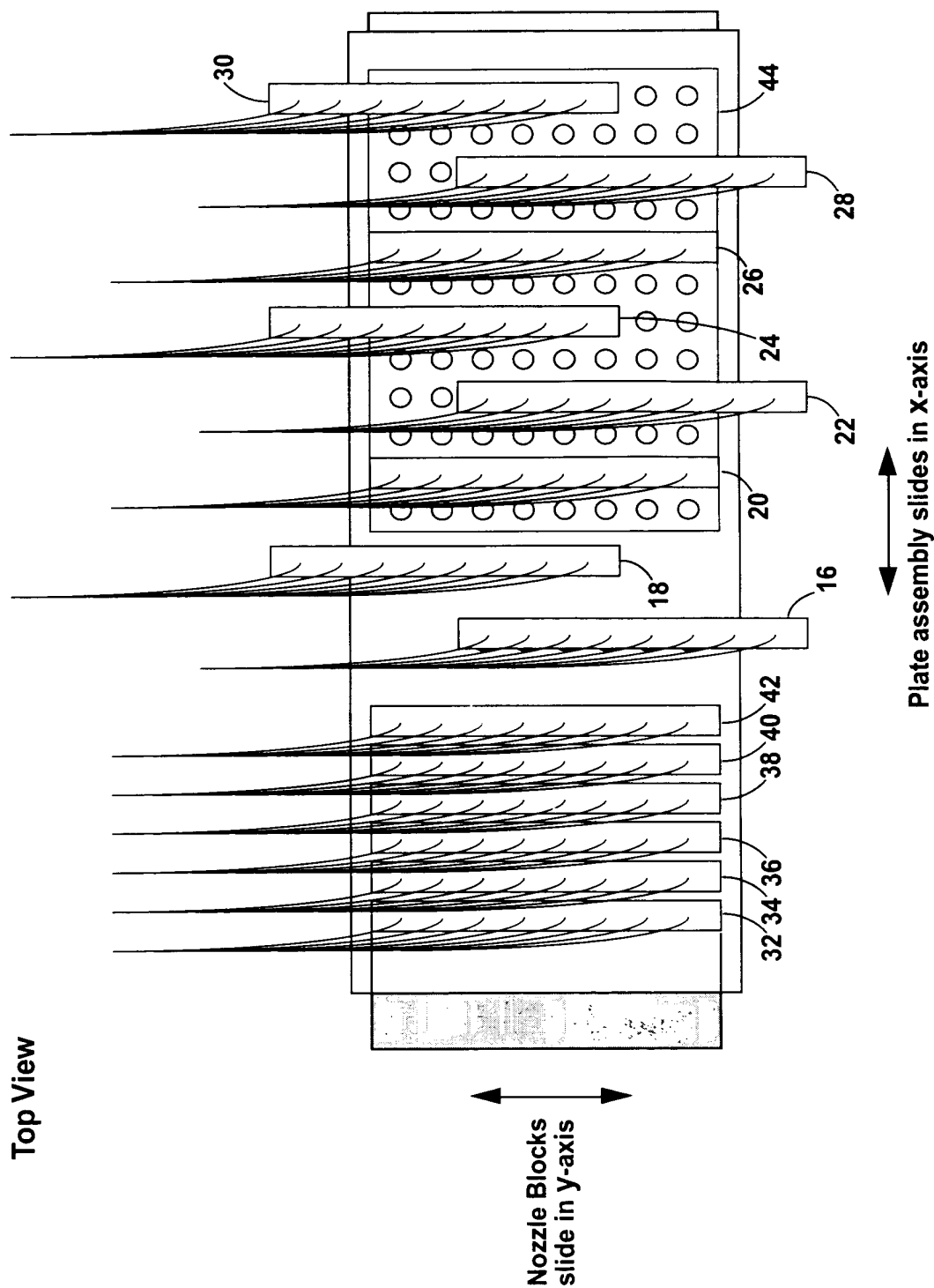


Figure 33



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Synthesis of Hydroxamic acids from alcohol resin

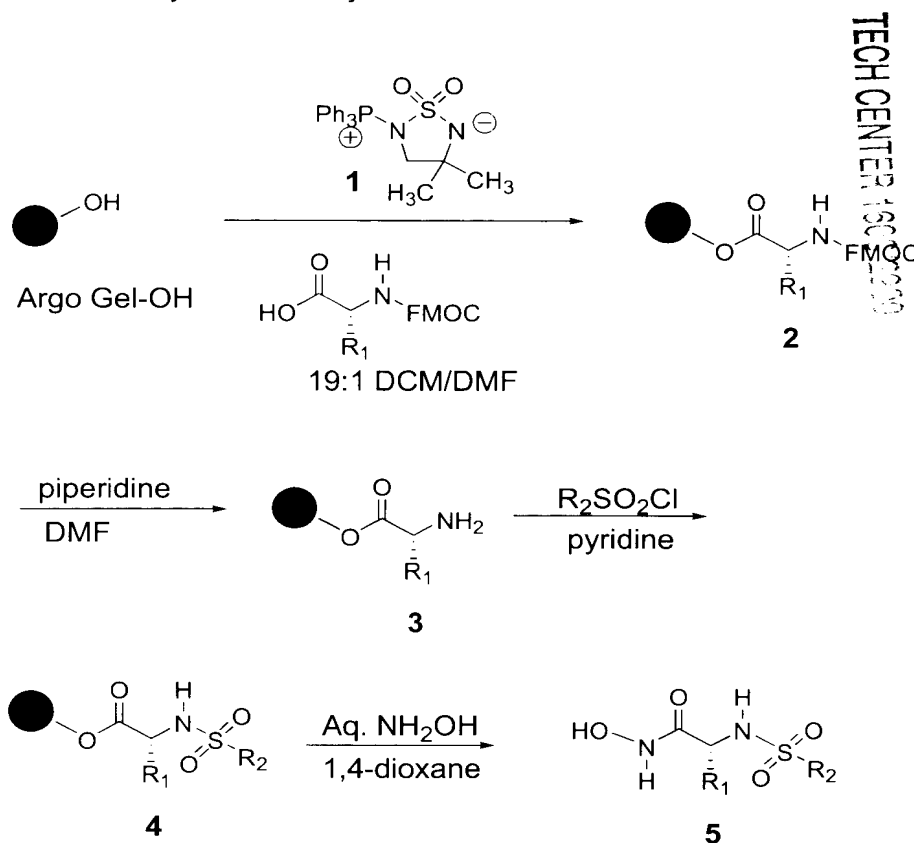


Figure 34



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Synthesis of hydroxylamine resin

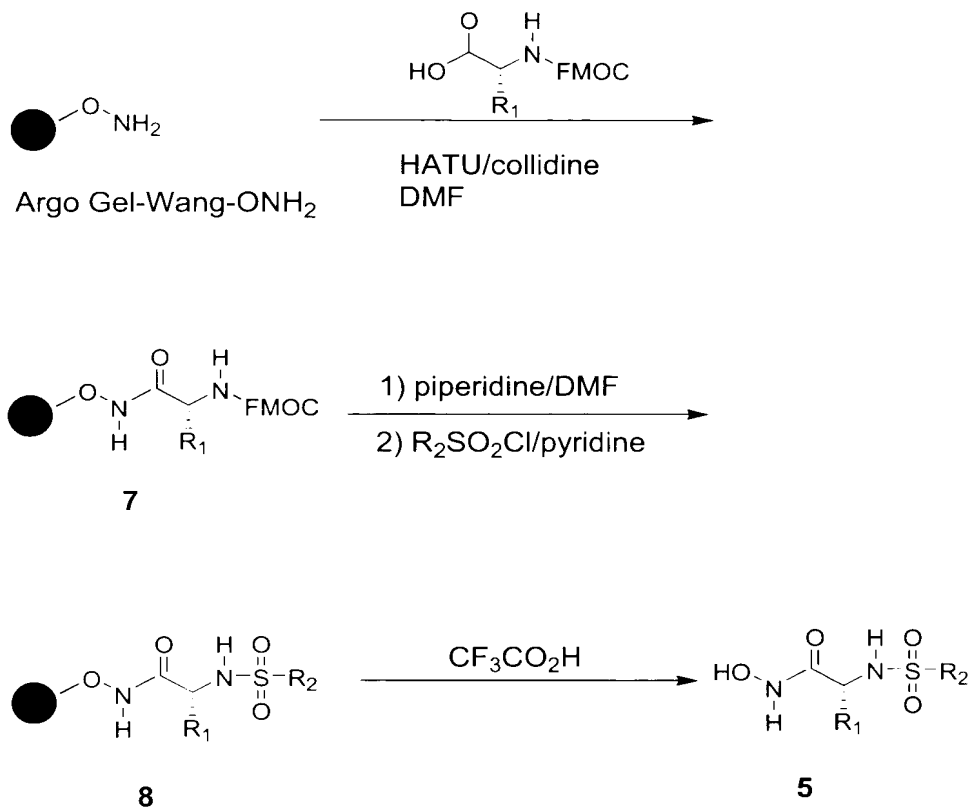


Figure 35

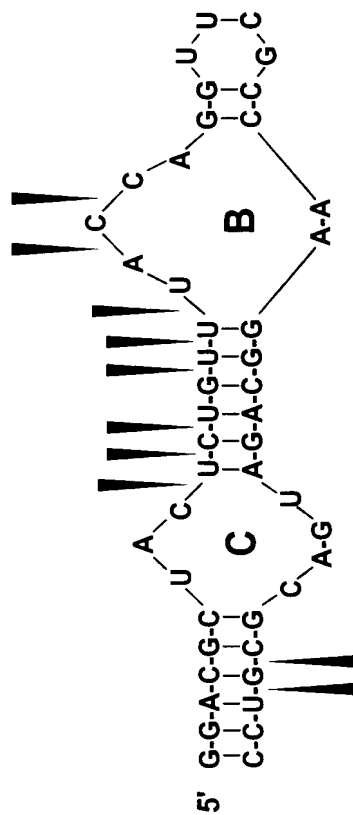


Figure 36



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ACD Code	Structure	Calc. ΔG of binding (kcal/mole)	IC ₅₀ (μM)
00001199		-5.1	< 2
00192509		-8.5	< 2
00003934		-5.1	< 50

Figure 37



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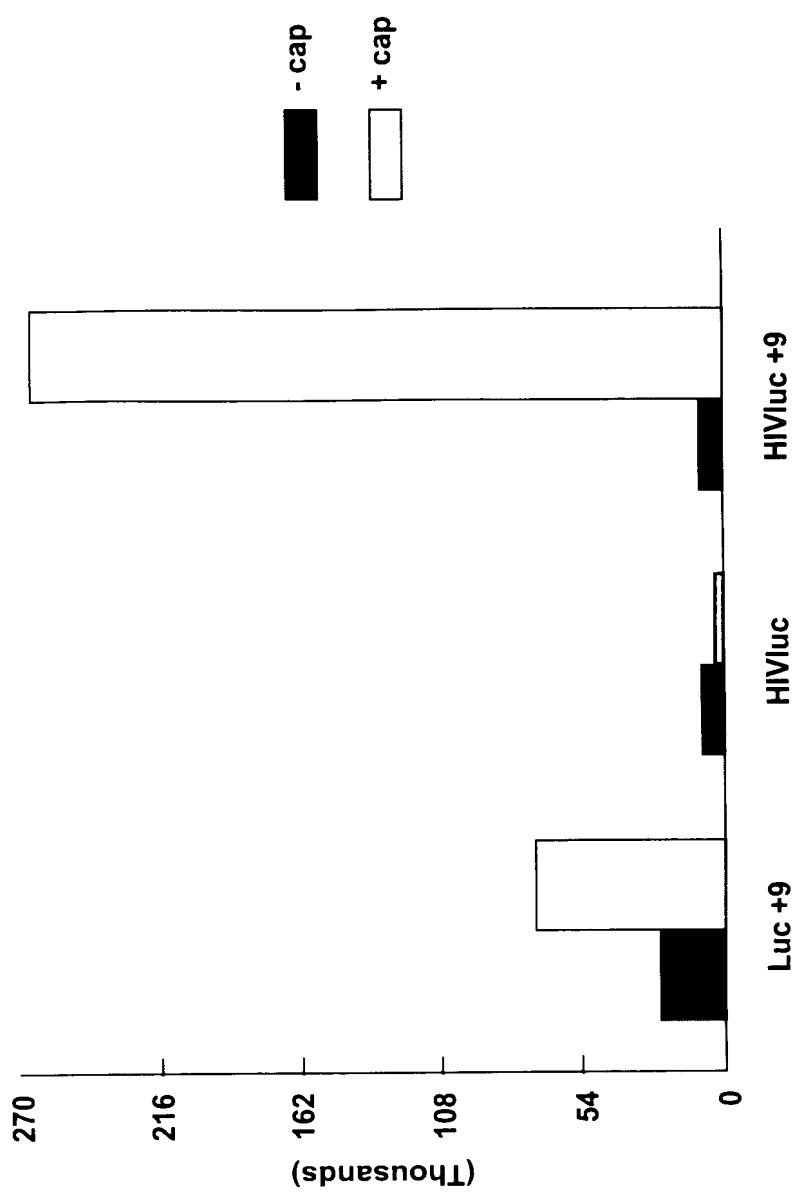
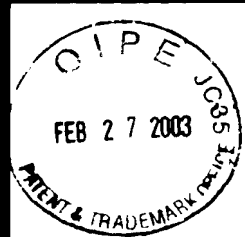


Figure 38A



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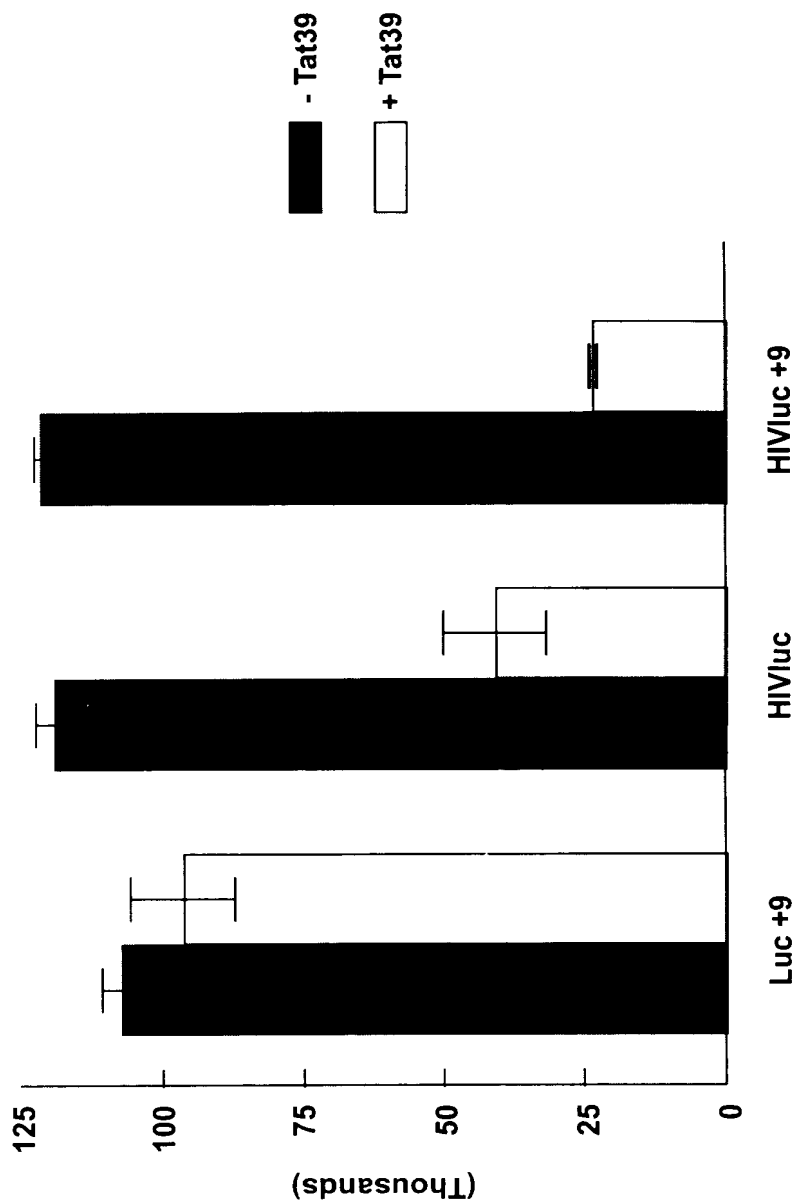


Figure 38B

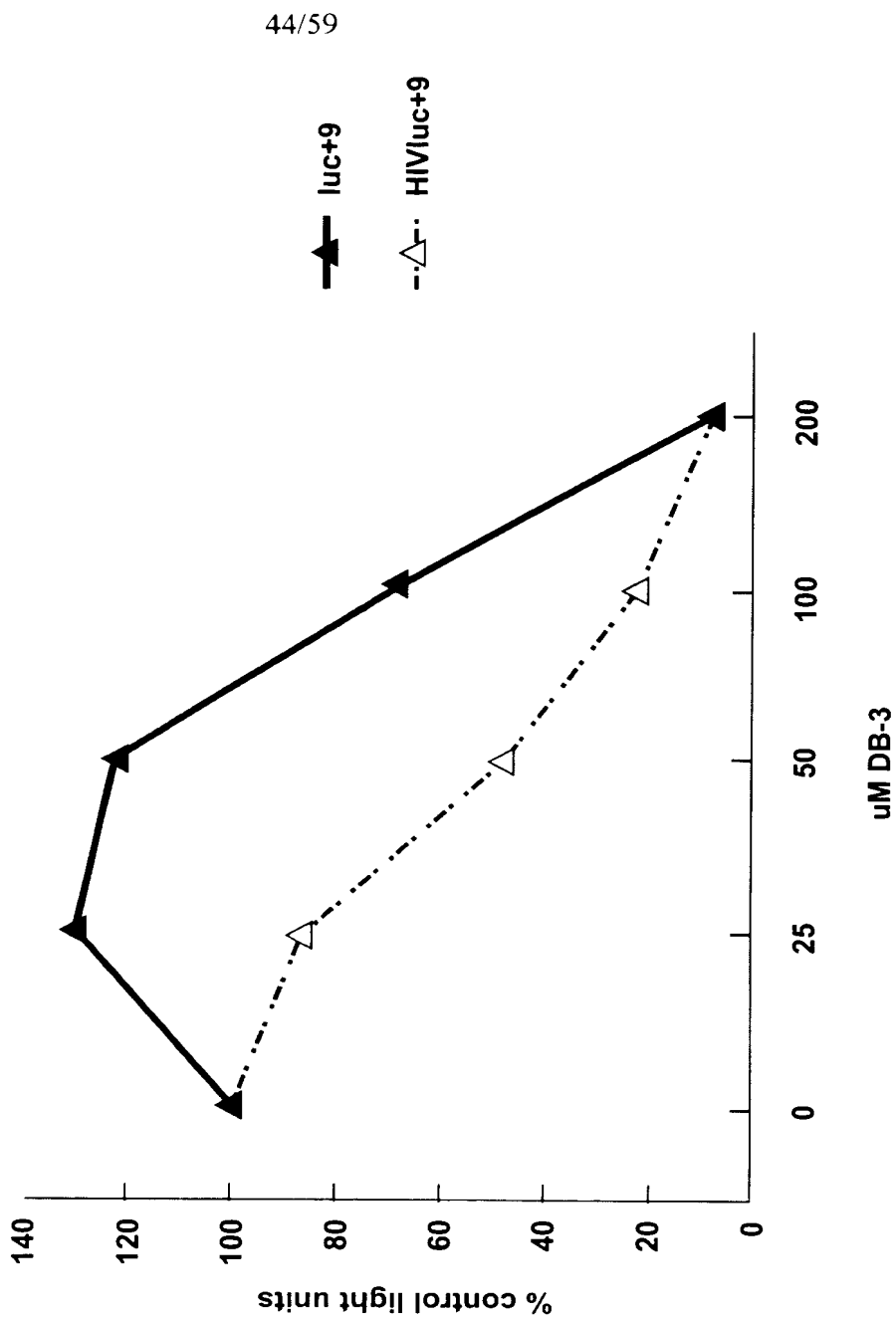


Figure 39

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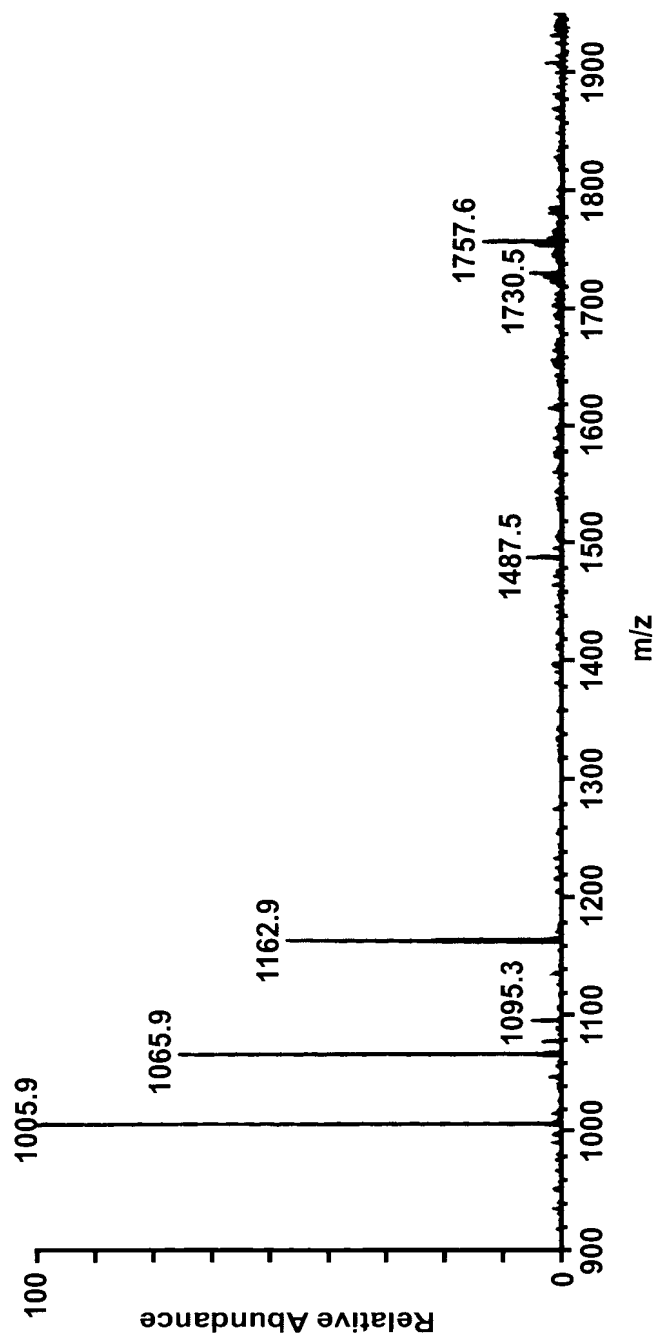


Figure 41A

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FEB 27 2003
PATENT & TRADEMARK OFFICE

Docket No.: IBIS-0007
App. No. 09/076,404
Filed: May 12, 1998
Title: Identification of Molecular Interaction Sites on RNA and Other Biomolecules
Inventors: Ecker et al.
Attorney: Jeffrey H. Rosedale
Sheet 47 of 59
Phone: (215) 568-3100

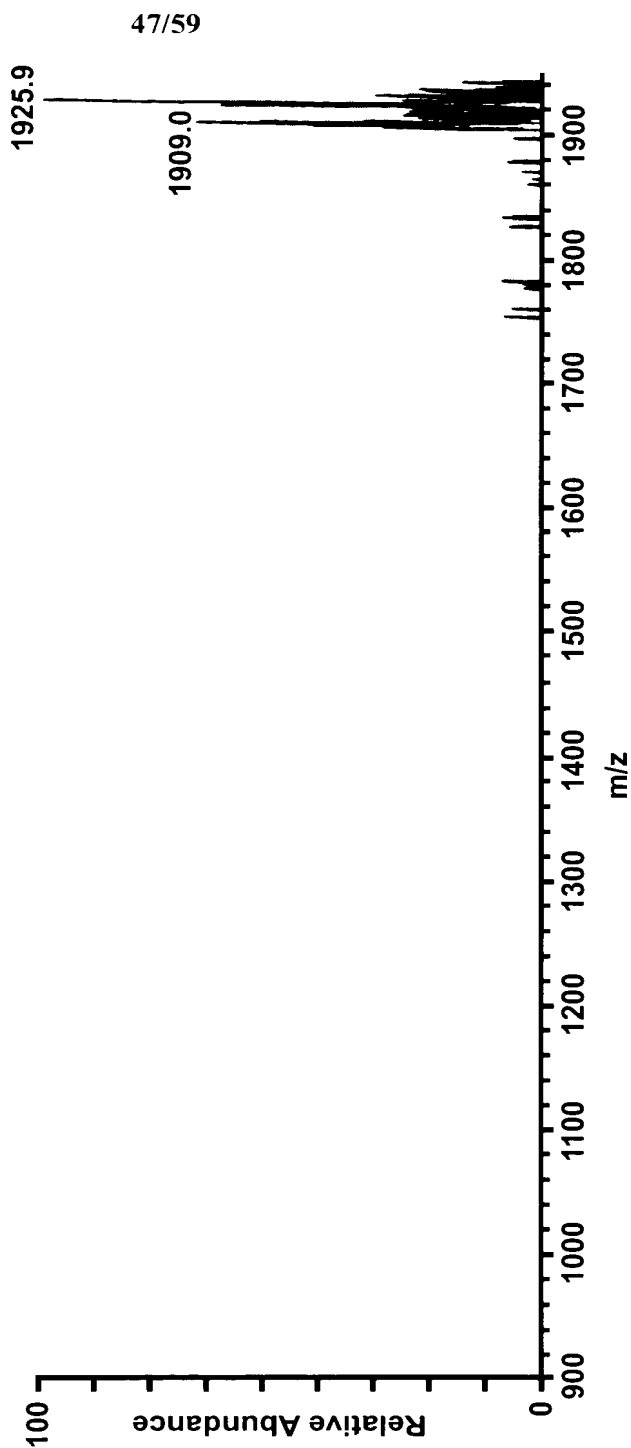


Figure 41B



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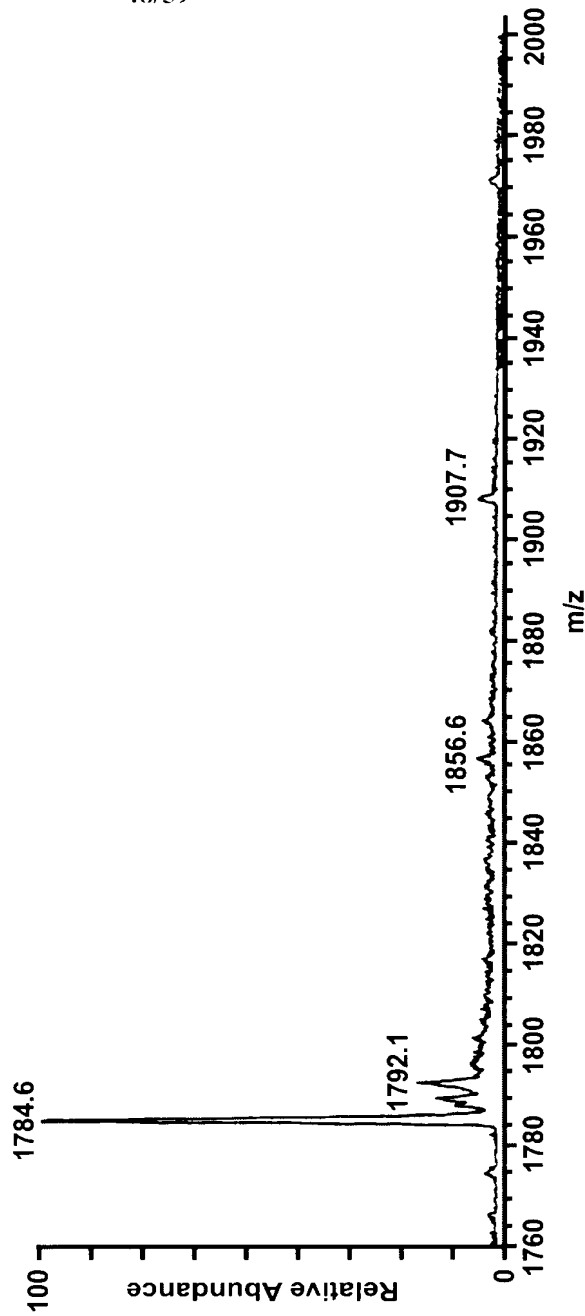


Figure 42A

O I P
FEB 27 2003
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Doc. No.: IBIS-0007
Appl. No.: 09/076,404
Filed: May 12, 1998
Title: Modulation of Molecular Interaction Sites on RNA and Other Biomolecules
Inventors: Ecker et. al.
Attorney: Jeffrey H. Rosedale
Sheet 49 of 59
Phone: (215) 568-3100

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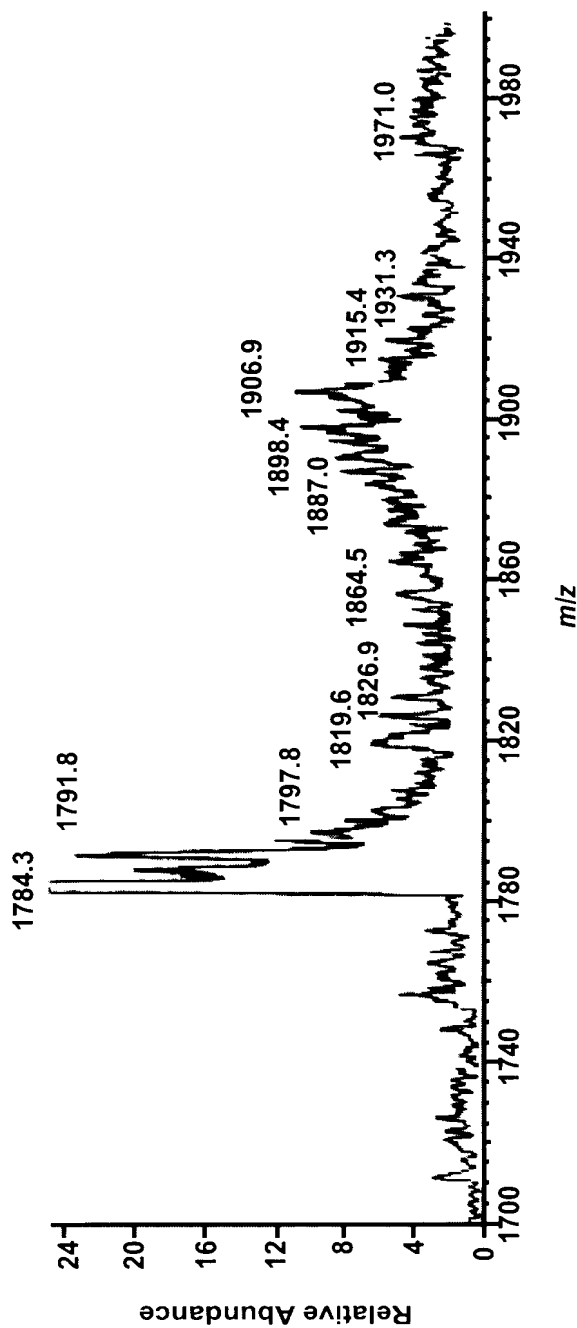


Figure 42B

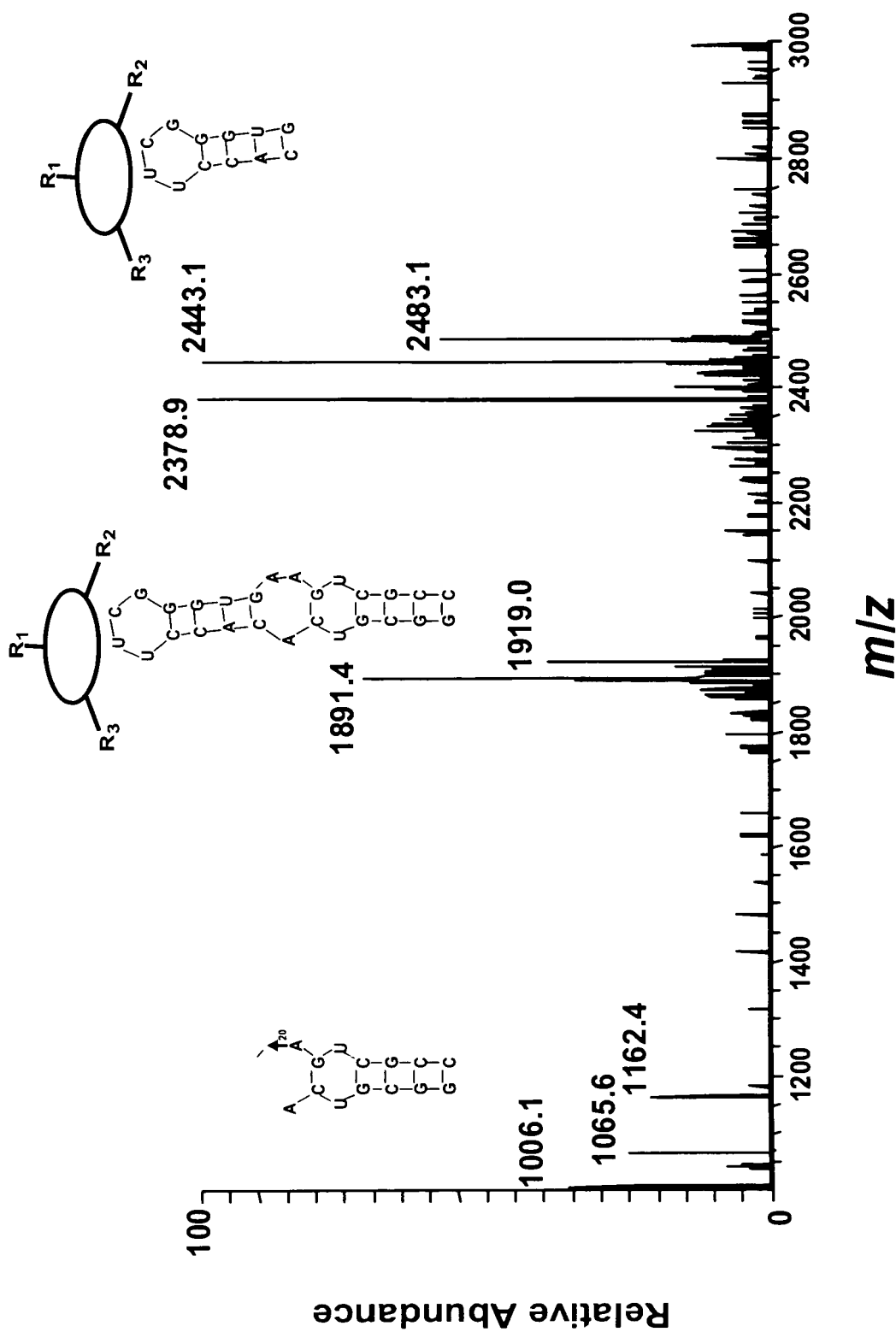


Figure 43

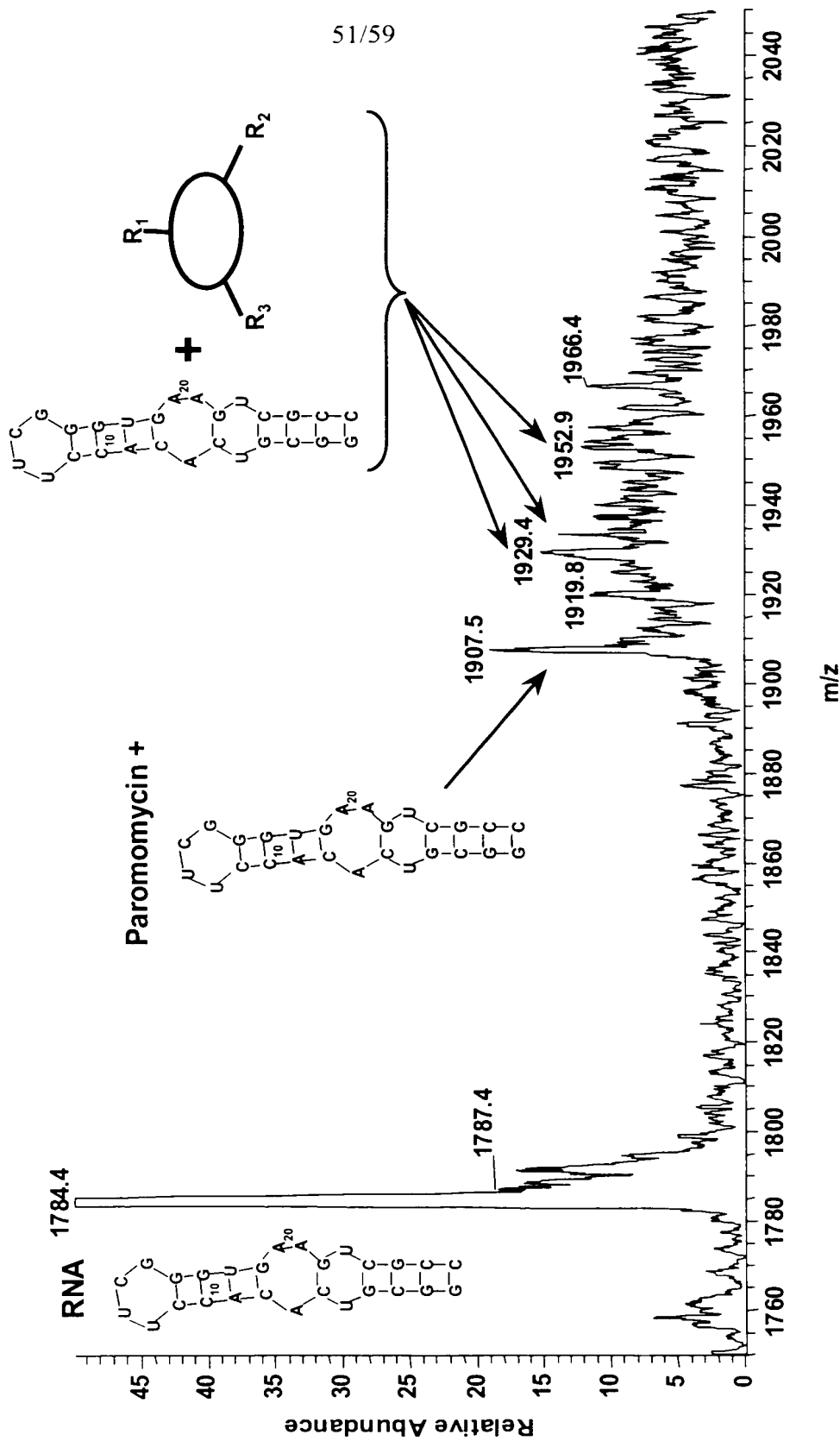


Figure 44



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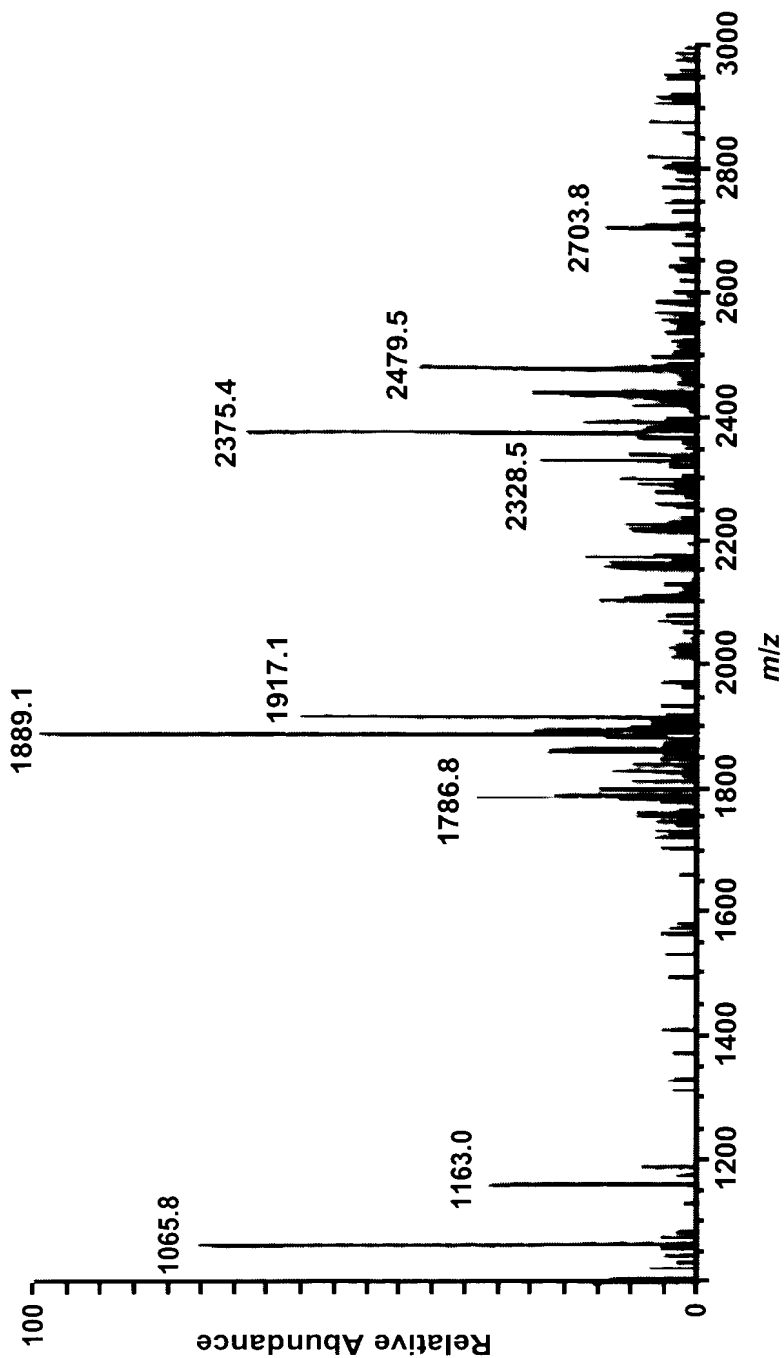


Figure 45

Figure 46